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GROUP 1600

Date

March 15, 1999

To

Examiner Gary Kunz

U.S. Patent and Trademark Office

Art Group: 1623

Washington, DC 20231

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From

Kathleen J. Philpot

Secretary to Janis K. Fraser, Ph.D., J.D.

Re

U.S. Patent Application No. 08/849,686

Attorney Docket No. 08269/003001

Courtsey Copy of Response to Examiner's Action

dated August 17, 1998

Number of pages including this page 15

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Art Unit: 1623

ATTORNEY DOCKET NO. 08269,

Examiner: Gary Kunz

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Arne Helge Deggerdal et al.

Serial No.: 08/849,686

Filed : August 21, 1997

Title : ISOLATION OF NUCLEIC ACID

Assistant Commissioner for Patents Washington, DC 20231

OFFICIAL

RESPONSE TO OFFICE ACTION DATED AUGUST 17, 1998

REMARKS

Reconsideration of the application is respectfully requested in view of the following remarks.

The Invention

The present invention includes a solid-phase method for nucleic acid isolation without using chaotropes, which are reagents that denature proteins. In this method, nucleic acids bind to a solid support made of an organic (i.e, carbon-based) polymer such as latex, polyurethane, or polystyrene, in the presence of a detergent and the absence of any chaotrope. A kit for practicing the method is also included within the scope of the invention.

Pending Claims

Claims 1-24 are pending and have been rejected on various grounds, discussed below.

> Date of Deposit I hereby certify under 37 CFR 1.8(a) that this correspondence is being deposited with the United States Postal Service as first class mail with sufficient postage on the date indicated above and is addressed to the Assignant Commissioner for Patents, Washingtop, D.C. 20231.

> > 03/15/99 MON 12:18 [TX/RX NO 6839] 20002



Rejection under 35 U.S.C. § 112, first paragraph (Pest mode)

Claims 1-24 are rejected for alleged concealment of the best mode contemplated by the inventors. Applicants respectfully traverse this rejection.

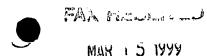
The Office Action refers to the following factual bases as evidence of concealment of the best mode:

> applicant's working examples employs exclusively DNA/Dynabeads DNA Direct™; 2) applicant has not specifically taught how to prepare the superparamagnetic polystyrene beads called DNA/Dynabeads DNA Direct™; and 3) applicant has not specifically disclosed the composition of the "Washing Buffer" on page 4, line 1 of the product instructions.

Applicants respectfully point out that these factual bases are not accurate nor should they be used as evidence for concealment of the best mode.

First, applicants' working examples employ types of Dynabeads[®] other than Dynabeads DNA Direct™. For instance, Examples 1, 2, 3, and 5 refer to the use of Dynabeads® M-280*, which are "obtainable by autoclaving a suspension of Dynabeads® M-280 tosylactivated" (page 19, lines 7-8); and Example 4 refers to the use of Dynabeads® M-450 uncoated (page 21, line 29). Therefore, the Dynabeads® products exemplified in the present specification represent different kinds of Dynabeads® and are not limited "exclusively" to Dynabeads DNA Direct™ as stated by the Examiner.

Second, the specification fully enables the preferred superparamagnetic particles disclosed. The specification states that Dynabeads® are especially preferred for the present



invention, i.e., "[t]he well-known magnetic particles sold by
Dynal AS (Oslo, Norway) as DYNABEADS, are particularly suited to
use in the present invention." (page 10, lines 36-37 and page 11,
lines 1-2). Both Dynabeads® M-450 and Dynabeads® M-280 were
publically available at the time the priority application was
filed, i.e., December 12, 1994. Evidence of the availability of
these Dynabeads is provided by the attached copy of Dynal's 1989
Product List (Exhibit A). Furthermore, other superparamagnetic
particles (sold by Promega Corporation) were also available at
the priority date, and have been shown to be suitable for use in
the claimed methods. See the copy of Promega's 1991 Protocols
and Application Guide for Streptavidin paramagnetic particles
attached as Exhibit B.

enabled because "applicant has not specifically taught how to prepare the superparamagnetic polystyrene beads called DNA/Dynabeads DNA Direct^M." This assertion premises on the Examiner's assumption that all working examples use exclusively Dynabeads DNA Direct^M. In view of the above discussion, such assumption is unfounded. Dynabeads DNA Direct[©] is not the exclusively exemplified and preferred embodiment, as characterized by the Office Action, given that other Dynabeads[©] products sold by Dynal AS are specifically taught in the specification as preferred embodiments. Therefore, whether the best mode of the present invention is enabled does not depend on whether Dynabeads DNA Direct[©] is enabled.



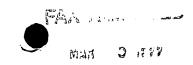
MAR 15 1999

That said, Applicants submit that Dynabeads properties is in fact fully enabled. The specification teaches how to make both superparamagnetic particles and the coatings thereof. See page 10, lines 32-36 and page 11, lines 3-12 in the specification. These particles can be readily used to produce particles equivalent to Dynabeads DNA Direct™. The specification also teaches that the Dynabeads DNA Direct™ Kit contains beads equivalent to Dynabeads® M-280*, which as discussed above were taught in the specification as being generated from beads which were publically available at the time the priority application was filed. See page 23, lines 1-4 in the specification.

Therefore, the Dynabeads® included in Dynabeads DNA Direct™ were enabled and readily available to one skilled in the art at the time the priority application was filed.

Third, contrary to the Office Action's assertion that "Washing Buffer" is part of the best mode, the "Washing Buffer" is merely a regular buffer used in an optional "washing step" for the purpose of convenience. This is evidenced from the specification teaching:

Although not necessary, it may be convenient to introduce one or more washing steps to the isolation method of the invention, for example following separation of the support from the sample. In the case of magnetic beads, this may conveniently be done before releasing the DNA from the beads. Any conventional washing buffers or other media may be used. Generally speaking, low to moderate ionic strength buffers are preferred, e.g., 10 mM Tris-HCl at pH 8.0/10mM NaCl. Other standard washing media, e.g., containing alcohols, may also be used, if desired. (page 11, lines 36-37 and page 12, lines 1-9 in the specification).



Therefore, use of a washing buffer was not contemprated by the applicants as essential or critical for the present invention. Even if it were, suitable washing buffers were fully disclosed. Thus, the kit's "Washing Buffer" is not part of the best mode.

In summary, the present invention discloses the preferred embodiments and fully teaches how to make and use such preferred embodiments. Withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 112, first paragraph (enablement)

Claims 1-24 stand rejected as being allegedly not enabled. This rejection is respectfully traversed.

The Office Action objects to the breadth of the claims with respect to "any and all organic solid supports." It states

The artisan would find it incredible that any and all organic solid supports would bind DNA and permit elution of DNA in view of applicant providing working examples using a single solid support, i.e., DNA/Dynabeads DNA Direct.

It has long been held by the Court of Appeals for the Federal Circuit and its predecessor that

A specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of §112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. "In re Brana, 34 USPQ2d 1437, 1441 (Fed. Cir. 1995) citing In re Marzocchi, 169 USPQ 367, 369 (CCPA 1971)

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According to the enablement standard set forth by the Court in In GROUP 1600 re Brana, the present invention is fully enabled.

First, the specification teaches that many different kinds of useful solid supports can be used for the present invention. See the following quotation from page 9 of the specification:

The solid support may be any of the well known supports or matrices which are currently widely used or proposed for immobilisation, separation etc. These may take the form of particles, sheets, gels, filters, membranes, fibres, capillaries, or microtitre strips, tubes, plates or wells etc.

Conveniently the support may be made of glass, silica, latex or a polymeric material.

While the present claims are limited to a solid support comprising an organic polymer, the above does serve to indicate the broad scope of materials which are taught as being useful. The specification further states, at pages 10 and 11, that many different types of surfaces have in fact been used successfully:

Non-magnetic polymer beads suitable for use in the method of the invention are available from Dyno Particles AS (Lillestrøm, Norway) as well as from Qiagen, Pharmacia and Serotec . . . Especially preferred are superparamagnetic particles for example those described by Sintef in EP-A-106873 . . . The well-known magnetic particles sold by Dynal AS (Oslo, Norway) as DYNABEADS are particularly suited to use in the present invention . . . Weakly and strongly positively charged surfaces, weakly negatively charged neutral surfaces and hydrophobic



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surfaces eg. polyurethane-coated have been shown to work well.

GROUP 1600

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Second, the specification also exemplifies multiple solid supports by using different Dynabeads. For instance, Examples 1, 2, 3, and 5-13 use Dynabeads. M-280* (page 19, lines 7-8 and page 20, line 19), while Example 4 uses Dynabeads. M-450 Uncoated (page 21, line 29). These different types of Dynabeads. utilize different surface materials, i.e., polyurethane and epoxy, and thus demonstrate that a variety of organic solid support materials can be used to practice the present invention.

Third, Applicants have tested a number of other surface materials having weakly negative to positively charged surfaces, including the following:

- (1) a mixture of diidocyanate/diethyleneglycol/ tetraethyleneglycol and 1,8-diamino-3,6-dioxaoctane;
- (2) a mixture of polyurethane and 1,8-diamino-3,6-dioxaoctane;
 - (3) a hydrolysed silane epoxy; and
- (4) a mixture of polyurethane and jeffamine (PEG600 with amine).

All of these were found to absorb DNA when used in the claimed methods.

To justify the rejection, the Office Action merely states, without support, that "[t]he artisan would find it incredible that any and all organic solid supports would bind DNA and permit elution of DNA." As stated above, the PTO has the initial burden of challenging a presumptively correct assertion



of utility in the disclosure. The specification weaches that any known solid supports containing an organic polymer can be used to isolate nucleic acid from a sample. The specification discloses and exemplifies a variety of such solid supports suitable for the present invention. In the absence of any evidence showing that one of ordinary skill in the art would reasonably doubt the applicants' teaching, the specification teaching "must be taken as in compliance with the enabling requirement." Id. The Office Action simply states a speculation and fails to make a prima facie nonenablement case. Therefore, the rejection is unfounded, and its withdrawal is respectfully requested.

CONCLUSION

Applicants submit that the grounds for rejection asserted by the Examiner have been overcome, and that the claims, as now pending, define subject matter that is fully enabled. On this basis, it is submitted that allowance of this application is proper, and early favorable action is solicited.

A Petition for Extension of Time and a check covering the extension fee are enclosed herewith.



Please charge any additional fees, or apply and 1999 credits, in this matter to Deposit Account No. 06-1950UP 1600 referencing attorney docket no. 08269/003001.

Respectfully submitted,

Date:

Janis K. Fraser, Ph.D., J.

Reg. No. 34,819

Fish & Richardson P.C. 225 Franklin Street Boston, MA 02110-2804

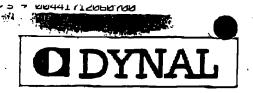
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EXHIBIT A







Enel. 1

PRODUCT LIST 1989



DYNABEADS™ products are based on extremely uniform, superparamagnetic polystyrene beads. Consisting of a maghemite (Fe₂O₃) containing core covered with a polymer, they have a smooth surface that is easily coated with antibodies or other selecting molecules. Combined with a magnet, Dynabeads make a unique tool in positive or negative separationes.

Fields of applications include: Immunology, Tissue Typing, Cancer research, Transplantation medicine, Microbiology, Virology, DNA Technology and Clinical chemistry.

DYNABEADS UNCOATED	Prod.no.	Volume
A. Immunomagnetic beads for cell separations. Uniform, superparamagnetic polystyrene beads with diameter 4.5 micron (c.v.< 5%). 4x10s DYNABEADS per ml (30 mg per ml) in aquous solution.		
For physical adsorption of primary antibodies of the IgM class, or for customer's own secondary antibodies. Primary monoclonal antibodies of the IgG class should be bound to Dynabeads M-450 via a secondary antibody for optimal function.	140.01 140.02	2 ml 10 ml
DYNABEADS M-450 Tosylectivated For convenient <i>chemical</i> coupling of proteins or secondary antibodies of customers own choice.	140.03 140.04	2 ml 10 ml
B. Immunomagnetic beads for use In microbiology and immuno- assays. Uniform superparamagnetic polystyrene beads with a polymer surface having only primary OH groups and with a dia- meter of 2.8 micron (c.v.< 3%). 6-7x108 DYNABEADS per ml (10 mg per ml) in aquous solution. EW DYNABEADS M-280 Tosylactivated For convenient chemical coupling of proteins, peptides or second-	í	·
ary antibodies of customers own choice. Dynabeads M-280 are activated by use of p-toluene suphonyl chloride and ready for coating through a simple incubation.	142.03 142.04	2 ml 10 mi

EXHIBIT B

609-274-4330

Pelephone lol Free

62067092 608-273-6967

600-356-9626

Madison, WI 53711-5399 USA

800-356-9526

2800 Woods Hollow Road

Promega Corporation

and Applications Gu omega Protocols

Second Edition

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Part Number Y991

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Nucleic Acid Detection, Purification and Labeling

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		ded ONA Primers
		B. Addition of (a. *P)Cordycepin-5'-Triphosphate to 3' Termini of Single-Stranded DNA Primers.
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*	Ħ.	Additional Nucleic Asid Labeling Literature Avaisable from Promaga
		Protocols for the following protein detection and puritication applications are provided elsewhere in this guide:
		Immunosereacing of Lembda Expression Libraries with the ProteBiote Immunocreening System

particles to the affinity purification of polyadenylated system. Unlike procedures which use direct coupling systems use a biolinylated otigonucleotide probe to mRNA with the PolyATractru system and to cDNA coupled streptavidia paramagnetic particles. This Promega has extended the use of paramagnetic hybridize in solution to the targeted mucleic acid. of probes to paramagnesic particles (6.7), these approach combines the spead and efficiency of solution hybridization with the convenience and syninesis and cloning with the Capture Clone? The hybrids are then captured using covalently speed (<1 minute) of magnetic separation.

for the production of the particles. These streptavidin specific aligonucteatide prabe used. For biolinylated oliga(dT), the calculated binding capacity is roughly Promega utilizes its own highly punited streptavidin and low non-specific binding of nucleic acids. The binding capacity for biolinylated oligonucleotides paramagnelic particles (SA-PMPs) exhibil a high binding capacity of the particles varies with the nmale probe captured/mg SA-PIAPs.

used in the development of immunoassays (5), probe

diagnostic assays (6), and for measuring RNA in cell lysates using dA-tailed capture probes (7)

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equipment. These particles have been successfully

Promega

Particle

fron exide into submicron sized particles which have

fication protocols. Paramagnetic particles incorporate

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messenger FMA (mRNA) by hybridization to the 3'

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as the solid support of choice for many affinity puri-

The attachment of nucleic acids to solid supports such nucleic actos. One common application of immobilized many applications in the field of molecular biology as nitrocellulose (1,2) and cellulose (3) has found particularly for affinity purification of proteins and nucleic acids is oligo(dT) cellulose purification of Macromolecules

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PATENT
ATTORNEY DOCKET NO. 08269/003001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Arne Helge Deggerdal et al.

Art Unit: 1623

Serial No.: 08/849,686

Examiner: Gary Kunz

Filed :

: August 21, 1997

Title

: ISOLATION OF NUCLEIC ACID

Assistant Commissioner for Patents Washington, DC 20231

PETITION FOR ONE-MONTH EXTENSION OF TIME

Pursuant to 37 C.F.R. 1.136, applicants hereby petition that the period for response to examiner's action mailed August 17, 1998, be extended for one month to and including December 17, 1998.

Enclosed is a check for \$110.00 for the required fee. Please apply any other charges or any credits to our Deposit Account No. 06-1050.

Respectfully submitted,

D-+-

De 16, 1998

danis K. Fraser, Ph.D., J.D.

Reg. No. 34,819

Fish & Richardson P.C. 225 Franklin Street Boston, MA 02110-2804

Telephone: 617/542-5070 Facsimile: 617/542-8906

343511.B11

Date of Deposit

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